UNITED STATES DISTRICT COURT
MIDDLE DISTRICT OF FLORIDA
TAMPA DIVISION

RUSSELL BULOW and ERNA BULOW,

Plaintiffs,

v. CASE NO. 8:18-cv-1781-WFJ-AEP

UNITED STATES OF AMERICA,

Defendant.
_____/

ORDER

The Court presided over the four-day non-jury trial held in June 2021.[1] The Court carefully considered all the pleadings, testimony, and other evidence, together with the post-trial written closing arguments with proposed findings of fact and conclusions of law (Dkts. 111, 112, 113, 114).

In this medical malpractice action against the Veterans Health Administration under the U.S. Department of Veterans Affairs ("VA"), Plaintiffs seek eight million dollars in damages for breach of the physician's standard of care concerning the continued use of Depakote[2] relative to Russell Bulow's acute

[1] The trial transcript is found at dockets 104 through 107. Citations to the trial transcript will be denoted Tr. Day "#" at "page numbers and lines."
[2] Depakote (or divalproex) is a mood stabilizer, which was referred to throughout the trial as either Depakote or valproic acid or valproate. Tr. Day 1 at 8:17-19 (Depakote is the brand name and the generic is valproate, divalproex, or valproic acid); 11: 15-16 (Depakote or divalproex); 46:22 (valproic acid or Depakote); Tr. Day 1 at 113:2-6; Tr. Day 2 at 187:6-23 (Depakote is mood stabilizer, not antidepressant).

pancreatitis. The issues are 1) whether in November 2015, the treating physicians at the Bay Pines VA breached the standard of care by failing to consider and determine Depakote as the cause of Mr. Bulow's acute pancreatitis and by failing to discontinue Mr. Bulow's use of Depakote upon his November hospital discharge, and 2) whether the breach constituted the legal, proximate cause of Mr. Bulow's second episode of acute pancreatitis on December 7, 2015.

The Court determines the VA physicians did not breach the applicable standard of care, nor did the Plaintiffs prove either general or specific causation attributable to the continued use of Depakote after the November 2015 hospital admission. The Court need not reach the issue of damages. Judgment is due to be entered for Defendant.[3]

FINDINGS OF FACT[4]

Based on the testimony of the eleven witnesses and the evidence admitted, the Court makes the following findings of fact.[5]

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[3] This memorandum decision contains the respective findings of fact and conclusions of law in separate sections. Fed. R. Civ. P. 52(a)(1) ("[T]he court must find the facts specially and state its conclusions of law separately."). The findings of fact must be set forth in "sufficient detail to indicate the factual basis for the ultimate conclusions of law." *Compulife Software Inc. v. Newman*, 959 F.3d 1288, 1308–09 (11th Cir. 2020) (quotation omitted).

[4] To the extent that any of the Court's findings of fact may be considered conclusions of law, or vice versa, they should be considered as such.

[5] Both Russell Bulow and Erna Bulow testified. Seven additional fact witnesses took the stand: Dr. Angelo Fernandes (gastroenterologist), Dr. Sanja Barrie (hospitalist), Dr. George Fawcett (emergency medicine), Dr. Edwin F. Lopez-Chaves (hospitalist), Mark Welvaert (wound care nurse), Dr. Harvey Tatum (gastroenterologist), and Dr. Robert Smeed (psychiatrist). Plaintiffs called two expert witnesses: Dr. Steven Freedman (gastroenterologist) and Dr. Gerald Smetana

1. Mr. Bulow was born in August 1958 and was 63 years old at the time of the trial. Tr. Day 2 at 160:23-25; 161:1-2. Russell Bulow married his wife Erna Bulow in 1989. Tr. Day 2 at 161:3-8., Tr. Day 4 at 15:1-16:14. They have four children. Tr. Day 4 at 16:2-5.

2. Mr. Bulow grew up in Portland, Oregon, and joined the United States Marine Corps upon graduation from high school. After serving, he took various jobs and ultimately worked for a company in Portland. After Mr. Bulow lost his job in 2007 and thereafter won a lawsuit against his former employer, the Bulows moved to Cape Coral, Florida in 2010. Mr. Bulow was unemployed and enrolled in a one-year business program at Cape Coral Tech. After completion of the program, he was unable to pass the math portion of the TABE test, a basic knowledge test, and remains unemployed. Tr. Day 2 at 182:16-183:5; 183:10-23; Tr. Day 3 at 171:2-18; Ex. 10A at SC-0012-16; Tr. Day 4 at 16:15-17:1.[6]

3. In 2015, the Bulows moved to St. Petersburg, Florida. Tr. Day 2 at 182:16-17; 188:21-22. Mr. Bulow first developed acute pancreatitis on November 16, 2015 and was hospitalized at the Bay Pines VA for almost three days. Ex. 19A at BPVA 4686-4689. Mr. Bulow had a recurrent bout of acute pancreatitis in December 2015, with severe complications and an extended hospitalization (at

(internal medicine). Defendant presented two expert witnesses: Dr. Daniel Buffington, Ph.D. (clinical pharmacist) and Dr. Scott Tenner (gastroenterologist).

[6] All exhibits ending in A, such as Ex. 9A, are Defendant's exhibits. All are found at docket 102.

least six months). *See* Tr. Day 2 at 196:2-199:8. The Bulows moved to Arizona in 2017 and then to Oklahoma in late 2018. Tr. Day 3 at 69:6-13; 73:22-74:7. In February 2019, Mr. Bulow had to have his gallbladder removed and suffered severe septic shock. Tr. Day 3 at 121:10-19. His medical problems continued.

I. MR. BULOW'S MEDICAL HISTORY

The following relevant, but lengthy, medical history of Mr. Bulow provides context in ruling on the issues presented. While the physicians handling the emergency presented in November 2015 may or may not have known all of these details, the information is beneficial in understanding when and why Mr. Bulow was placed and continued on Depakote, in determining the periods Mr. Bulow took the medication, and in showing the progressive decline of Mr. Bulow's overall health.

A. Before 2011 (Portland)

4. Mr. Bulow began smoking cigarettes in the 1980s. For years Mr. Bulow abused alcohol until he quit drinking in 2013. He has had sleep apnea since 2002, and severe sleep apnea since 2013, as well as memory and concentration problems. Ex. 9A at PVA-538; Ex. 19A at BPVA-04985-04987. He has suffered with back, shoulder, neck, knee, and hip pain. Ex. 9A at PVA-0404-0409; Ex. 15A at SSA-0038-49; Ex. 19A at BPVA-05086-05088; Tr. Day 3 at 146:20-149:25. He experienced chronic abdominal pain and severe diarrhea on a

daily basis for roughly ten years prior to September 2015, often making it impossible to leave the house before noon.[7] Ex. 9A at BPVA-04801-4804; Ex. 9B at PVA-0337-0341; Ex. 15A at SSA-0047; Tr. Day 3 at 142:20-144:24; 178:5-12. He reported years of sexual dysfunction.

5. Mr. Bulow has had a long history of mental health issues, which drastically limited his quality of life years before he developed pancreatitis in November 2015. He was first diagnosed with PTSD (non-military related) in 1995 or 1996 in Portland, Oregon. Ex. 19A at BPVA-5065; Ex. 9A at PVA-356. Mr. Bulow began psychiatric treatment in 2002 at the VA in Portland when he was originally seen for PTSD. Ex. 9A at PVA 0443-0449. Mr. Bulow testified that he started suffering from depression a few years prior to 2002. He recalled confusion and trouble concentrating, and his wife thought he was angry all the time. The VA prescribed antidepressants and mood stabilizers. Tr. Day 2 at 184:1-185:17; Tr. Day 3 at 10:4-19; 167:25-168:6.[8] There is no evidence that Mr. Bulow was

[7] On November 6, 2015, Mr. Bulow's colonoscopy confirmed lymphocytic colitis, which is an inflammatory condition in which the colon lining is infiltrated by immune system cells, leading to chronic diarrhea. Tr. Day 1 at 55:6-13; 56:16-57:7.

[8] In the past, Mr. Bulow suffered at least three head traumas, with possible brain injuries. Mr. Bulow testified about (1) being assaulted in boot camp while in the Marines, which is when he thinks his PTSD started, (2) being hit in the head with a coffee mug on a boat in San Francisco, and (3) being in a bar fight in Oregon. Tr. Day 3 at 134:2-135:9. Mr. Bulow, however, disputed that he had suffered any brain trauma or head injuries. Tr. Day 3 at 133:14-134:1 (Mr. Bulow noted that VA doctors years later "said I had head trauma" but "I don't know where they came up with brain trauma or head injuries"). Progress notes prepared by a VA geropsychiatry consult in March 2016 include the three events that Mr. Bulow described and state that "since the head traumas, [Mr. Bulow] reports difficulty remembering events." Tr. Day 3 at 135:10-135:17;

placed on Depakote at this time.

6. Similarly, a 2002 mental health progress note states "he has a loss of interest and pleasure in his life, gets road rage and is irritable, but since he was started on citalopram these symptoms are somewhat better." The examination reported chronic PTSD symptoms, including numbing and avoidance, hyperarousal symptoms, easy to anger, some road rage, intrusive memories of being assaulted, and irritable mood. Tr. Day 3 at 168:7-169:9; Ex. 9A at PVA-0443-446. He complained of sexual dysfunction as early as 2002. Ex. 9A at PVA-447-448; Ex. 9A at PVA-357; Ex. 9A at PVA-209-210.[9]

7. After the Bulows moved to Florida in 2010 but before Mr. Bulow enrolled in the Fort Myers, Florida VA system, he saw his primary care physician at the Portland VA in 2011. Ex. 9A at PVA-201, 209-213. His physician noted on June 16, 2011, that Mr. Bulow reported binge drinking on the weekends, tobacco abuse, depression, issues with sleeping, and sexual dysfunction. Ex. 9A at PVA-210-213. Mr. Bulow declined to start a medication for depression because he

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136:1-18; Ex. 19A at BPVA-01791. Weighing the evidence, the Court accepts as true the medical observation and assessment that Mr. Bulow suffered three prior brain traumas and possible brain injury.

[9] A September 2007 progress note states:

> He feels like his thoughts are completely disorganized and he can't think clearly. Getting up in the morning is a difficult task and most days he can't even find energy to shower and get ready for the day. He has lost interest in all of his activities that he used to do (boating, hiking, spending time with his children). He has four children at home who he thinks he is letting down.

Tr. Day 3 at 169:10-170:4; Ex 9A at PVA -0357.

wanted to avoid even greater issues with his sex life. Ex. 9A at PVA-210, 213.

B. 2011 to 2015 (Florida)

8. Around the time Mr. Bulow could not pass the TABE test at Cape Coral Technical, Mrs. Bulow noticed his whole personality changed. Tr. Day 4 at 17:2-24. She testified that he reverted to not having much motivation. Tr. Day 4 at 43:17-25. Mrs. Bulow testified that her husband then started seeing a psychiatrist, Dr. Nelson Monroy, at the VA in Fort Myers, Florida, on a regular basis. Because Mr. Bulow wanted Mrs. Bulow with him all the time, she attended his appointments with Dr. Monroy. Tr. Day 4 at 17:25-18:9.

9. On January 25, 2013, Dr. Monroy noted that Mr. Bulow's chief complaint was that he had "been miserable for the last two years." Mr. Bulow reported probable ADHD (attention deficit hyperactivity disorder) and that his day was "hell" because he could not get organized. Tr. Day 3 at 170:5-171:1; Ex. 19A at 05065-5067. Dr. Monroy's impression included mood disorder, bipolar II disorder, ADHD, nicotine dependence (two packs per day), and PTSD per his documented medical history. Ex. 19A at BPVA-5065, 5067.

10. Mr. Bulow sought a second psychological opinion and made two visits to a private mental health facility in Fort Myers called SalusCare (also referred to as Ruth Cooper Center). Mr. Bulow expressed the same complaints including loss of enjoyment, inability to organize his thoughts, crying all the time, daily anger

outbursts, and lack of exercise and hygiene. Tr. Day 3 at 131:7-20, 171:2-172:14; Ex. 10A at SC-0012-0016-17 (2/8/2013 note of SalusCare). In February 2013, he was drinking four to eight shots of whiskey or rum per night. *Id*. Dr. Monroy reviewed the second opinion and noted only one difference—that Mr. Bulow was not considered to have ADHD. Ex. 19A at BPVA-5053 (3/4/2013 note of Dr. Monroy).

1. Prescribing Depakote

11. Mr. Bulow's treatment continued with Dr. Monroy. On April 3, 2013, Dr. Monroy prescribed Depakote. Ex. 19A at BPVA-5039. Although Mr. Bulow testified that Dr. Monroy first prescribed Depakote as a mood stabilizer in 2012, the medical records confirm the April 2013 start date. *Id*.; Tr. Day 2 at 185 25-186-7.[10] Weighing the evidence, the Court finds the April 3 date as the first date Mr. Bulow was prescribed Depakote.

12. Mr. Bulow tolerated Depakote, unlike antidepressants. Tr. Day 2 at 185:25-186:17 (Bulow).[11] In September 2013, Mr. Bulow's ability to concentrate was better and his mood was "improved by using Divalproex[.]" Tr. Day 3 at 174:10-24; Ex. 19A at BPVA-05005-05009 (9/3/2013 note of Dr. Monroy). By

[10] Depakote is a mood stabilizer that can also be used for seizures. Tr. Day 1 at 113:2-6. Depakote is not an antidepressant. Depakote was FDA-approved for use in bipolar disorder in about 1995. Tr. Day 4 at 79:11-82:18 (Buffington).

[11] In contrast to his medical records, Mr. Bulow testified that Depakote had caused him to feel bad and have erectile dysfunction. Tr. Day 2 at 186:18-187:5; Tr. Day 3 at 59:24-60:3.

February 2014, however, Mr. Bulow's depression worsened. Mr. Bulow reported his depression as seven to eight on a scale of ten and reported crying almost daily for more than three weeks. Tr. Day 3 at 174:25-176:5; Ex. 19A at BPVA-04956-4961 (2/3/2014 progress note).

13. In May 2014, Mr. Bulow applied for Social Security disability benefits. He filled out by hand the application, which similarly paints a bleak picture of his life prior to acute pancreatitis. Mr. Bulow wrote "Today my life is a living hell. I feel hopeless and sometimes think that maybe I would be better off dead just to have some relief from my miserable life. However, I do not think about killing myself because I still have hope that I can get better." Tr. Day 3 at 176:7-178:4; Ex. 15A at SSA-0047. He noted on the form he had "no energy" and angry outbursts. Tr. Day 3 at 178:13-179:6; Ex. 15A at SSA-0047. He spent most of his day watching, rewinding, and re-watching the same TV shows due to his lack of focus. Tr. Day 3 at 179:7-180; Ex. 15A at SSA-0047.[12]

14. Regarding medications, the 2014 application lists all his prescriptions

[12] As for responsibilities around the house, Mr. Bulow listed his sole chore as "a little pruning." Tr. Day 3 at 180:11-181:12; Ex. 15A at SSA-0040. Although Mrs. Bulow testified that he had maintained the yard, pressure-washed, and dealt with the cars, roof, leaves, and other household tasks up until his acute pancreatitis, she deferred to Mr. Bulow's handwritten 2014 application as more likely accurate. Tr. Day 4 at 44:1-6, 45:4-15, 45:21-46:7.

With respect to finances, Mr. Bulow testified that his wife had taken them over long before 2014, which is supported by the 2014 application. Tr. Day 3 at 183:2-8; 15A at SSA-0041. Mrs. Bulow testified that she guessed she had been mistaken when testifying that her husband had handled the finances before he got sick. Tr. Day 4 at 46:8-21. Understandably, both Mr. and Mrs. Bulow struggled to remember specifics from many years earlier.

including "2 tabs Divalproex 750 mg 24 hr." Ex. 15A at SSA-0046. Mr. Bulow testified that he took his medicine as prescribed. Tr. Day 2 at 190:5-20.

15. Mr. Bulow continued to see Dr. Monroy for his depression through March 2015. Mr. Bulow's antidepressant had been stopped prior to June 2014 "because of dry mouth." Tr. Day 3 at 183:9-22; Ex. 19A at BPVA-04906 (6/6/2014 progress note of Dr. Monroy). Throughout 2014, Mr. Bulow continued to harbor fleeting suicidal thoughts with no plans and to experience frustrations with sleep apnea, the inability to pass the TABE test, confusion, and irritability. Tr. Day 3 at 183:23-184:9; Ex. 19A at BPVA-04906; Tr. Day 3 at 184:10-185:1; Ex. 19A at BPVA-04863 (8/14/2014 progress note of Dr. Monroy). Nothing changed through his last visit with Dr. Monroy on March 12, 2015. Tr. Day 3 at 185:1-18; Ex. 19A at BPVA-04811. On that date, Mr. Bulow's current medications included Divalproex. Ex. 19A at BPVA-04812 ("Divalproex 500 mg 24hr (ER) SA tab take three tablets by mouth daily at bedtime for mood").

16. Mr. Bulow testified that in July 2015 he tapered himself off and stopped Depakote, after researching how to do so online. Tr. Day 3 at 60:8-15; Tr. Day 2 at 187:6-23. His wife testified that she was unaware he had weaned himself off of Depakote and unaware of exactly what medications he was taking. Tr. Day 4 at 18:10-22. After stopping Depakote, Mr. Bulow saved all of the excess bottles of pills. Tr. Day 3 at 60:16-25.

17. Mr. Bulow did not seek psychiatric care again until August 2015 when he transferred his treatment from Cape Coral to the Bay Pines VA in St. Petersburg.[13] Ex. 19A at BPVA- 4754-4758; Tr. Day 3 at 5:15-25; 6:15-23. On August 6, 2015, Mr. Bulow told Dr. Smeed that he had discontinued both valproic acid and paroxetine 2-3 months earlier. Tr. Day 3 at 7:24-8:9. Dr. Smeed testified that it is fairly common for patients with bipolar disorder to stop medications on their own when they are feeling better or more stable. Tr. Day 3 at 46:3-16. Dr. Smeed told him, and the Bulows agreed, to start the Depakote again, and Mr. Bulow filled the 30-day prescription (with three refills).[14] Ex. 19A at BPVA-4758 ("resume Depakote 500 mg BID for 1 week, then increase to 500 mg qam and 1000 mg qhs"); Tr. Day 3 at 48:2-9. Dr. Smeed expected Depakote to provide maintenance treatment for Mr. Bulow's bipolar disorder and to prevent further episodes of mania or hypomania.[15] Tr. Day 3 at 46:17. Dr. Smeed discussed the common risk factors of taking Depakote including liver

[13] The Bulows moved to St. Petersburg in May 2015 for financial reasons and to be closer to a hospital. Tr. Day 2 at 187:24-188:22; Tr. Day 4 at 21:5-7.

[14] Mr. Bulow was willing to resume Depakote at his wife's behest, but later admitted he felt better while taking it. Tr. Day 3 at 45:14-46:2.

[15] Hypomania is "a milder form of mania, meaning the patient may have an elevated mood, but it may not last as long" or be as severe as mania. Tr. Day 3 at 56:7-17. Hypomania may cause a decreased need for sleep, impulsive behavior, and irritable mood. *Id*. Mania "is more of a severe episode of bipolar disorder" lasting up to two weeks and results in hospitalization, legal consequences, or severe physical injury. Tr. Day 3 at 56:18-24. Mania usually involves grandiose thinking, irritable mood, decreased need for sleep, risk-taking behavior, flight of ideas, and pressured speech. *Id*.

toxicity, agranulocytosis, and decreased cognition. Tr. Day 3 at 18:20-20:6.[16]

18. Dr. Smeed believed he was aware of the black box warning on Depakote at the time but does not believe he discussed it with Mr. Bulow because it was not a common side effect. Tr. Day 3 at 20:7-22; 47:11-20. The black box warning provides in full:

> **Pancreatitis**
>
> Cases of life-threatening pancreatitis have been reported in both children and adults receiving valproate. Some of the cases have been described as hemorrhagic with a rapid progression from initial symptoms to death. Cases have been reported shortly after initial use as well as after several years of use. Patients and guardians should be warned that abdominal pain, nausea, vomiting, and/or anorexia can be symptoms of pancreatitis that require prompt medical evaluation. *If pancreatitis is diagnosed, valproate should ordinarily be discontinued*. Alternative treatment for the underlying medical condition should be initiated as clinically indicated.

Dkt. 111 at 4 (emphasis added); Tr. Day 2 at 120:21-121:10. The black box warning was added in 2000 by Abbott, the manufacturer. Tr. Day 4 at 79:24-81:15 (Buffington). A black box warning is an area formatted in a black box in the drug materials to highlight either contraindications, or warnings and precautions. Tr. Day 4 at 77:15-78:3. It is not "a higher level of warning." Tr.

[16] Dr. Smeed directed Mr. Bulow to follow up with his primary care physician, discussed the VA crisis hotline, and referred him for a neuropsychological evaluation to rule out a neurocognitive disorder related to the traumatic brain injuries. Dr. Smeed wanted Mr. Bulow to return in 6 weeks or sooner if needed. Tr. Day 3 at 16:5-8; 20:23-21:3; 7-10. Mr. Bulow did not keep his next appointment with Dr. Smeed or the scheduled September 2015 evaluation. Ex. 19A at BPVA-4734 (9/15/2015 gastroenterologist note); Tr. Day 3 at 21:7-15, 24:1-6; Ex. 19A at BPVA-04716.

Day 4 at 77:17. Dr. Buffington testified that Abbott's adding the black box warning for pancreatitis does not constitute a "declaration of causation for pancreatitis." Tr. Day 4 at 95:23-24.

19. On October 30, 2015, Mr. Bulow refilled the August 6 Depakote prescription with another 30-day supply. Tr. 3 at 47:21-52-10. Whether Mr. Bulow took the Depakote as prescribed by Dr. Smeed starting in August 2015 is inconclusive. Mr. Bulow testified that he augmented the August 2015 prescription with pills he previously accumulated and that he "always followed orders . . . always did my medication." Tr. Day 3 at 60:19-61:1-12. His 2015 Social Security application and his 2015 neuropsychological evaluation, however, contradict this testimony. Ex. 15A at SSA-0040; Ex. 19A at BPVA-04607. On other occasions Mr. Bulow stopped medication—paroxetine, Depakote, and bupropion. Tr. Day 3 at 7:24-8:9; Ex. 11A at SAZVA-1790-1793. The Court finds Mr. Bulow's testimony inconsistent. The Plaintiffs did not prove Mr. Bulow took Depakote as prescribed.

20. Mr. Bulow saw Dr. Smeed again on November 5, 2015. Tr. Day 3 at 22:4:4-23-1. After discussion with Mr. Bulow about how antidepressants made him feel ill, Dr. Smeed started risperidone, an atypical anti-psychotic approved for mood disorders, and continued Depakote. Tr. Day 3 at 22:4-23:25. The neuropsychological evaluation was rescheduled for November 25, 2015. Tr.

Day 3 at 24:1-6.; Ex. 19A at BPVA-4716 (Dr. Smeed's note of 11/5/2015). Mr. Bulow developed acute pancreatitis about ten days before the scheduled evaluation. Mr. Bulow did not develop acute pancreatitis during the time he had taken Depakote beginning 2013 until mid-November 2015. Tr. Day 1 at 196:17-19.

2. Weight Gain, Triglycerides, Diabetes, Smoking, Alcohol

21. Mr. Bulow started gaining weight in 2014 and became obese. Tr. Day 3 at 178:5-12; Ex. 15A at SSA-0047. At that time, he had high cholesterol and high triglycerides treated with fish oil and a statin, which lowers both cholesterol and triglycerides. Tr. Day 3 at 185:19-186:13; Ex. 19A at BPVA-04796-4800. He became a borderline diabetic in July 2015, and in October 2015, a month before he suffered the acute pancreatic attack, his condition worsened to overt diabetes based on his A1C value of 6.7. Tr. Day 2 at 90:23-91-20; Tr. Day 2 at 122:9-124:7; Ex. 19A at BPVA-04483. As early as April 2015, a VA pharmacist, Dr. Carmen Ahed, expressed her concerns and warned Mr. Bulow about acute pancreatitis. Tr. Day 3 at 186:14-187:14; Ex. 19A at BPVA-04796-4800.

22. Health records show that his triglycerides jumped from 114 in September 2012 to 481 in May 2013. 19A at BPVA-4959. In September 2013, his triglycerides were down to 213. In April 2014, his triglycerides were 471. In October 2014, his triglycerides were 502. Tr. Day 2 at 72:13-73:3; 73:8-74:5.

In March 2015, Mr. Bulow's triglycerides were 1,129 and his cholesterol was 251. 19A at BPVA-4797; Tr. Day 2 at 74:6-25. When Mr. Bulow became borderline diabetic in July 2015, his triglycerides were 370. Tr. Day 2 at 75:1-8; 19A at BPVA-4757. In October 2015, Mr. Bulow's triglycerides were 518. Tr. Day 2 at 75:12-76:4; 19A at BPVA-4564.

23. At the beginning of November 2015, Mr. Bulow rapidly gained ten pounds in eleven days.[17] Mr. Bulow's lab work in the hospital showed his triglycerides were 972, his liver enzymes were normal, and his Depakote level registered at only a therapeutic (not toxic) level. Tr. Day 1 at 36:14-17; 37:12-15; 38:13-39:1.

24. Both Mr. Bulow's medical records and testimony reflect that he had a smoking history of more than 35 years prior to his acute pancreatitis. Mr. Bulow testified that he smoked two packs a day for 20 years beginning around 1990, and one pack a day since about 2008. Tr. Day 3 at 124:18-127:16. *But see* Tr. Day 3 at 130:10-20; Ex. 19A at BPVA-05092-7 (in September 2011, his primary care physician noted he smoked two packs per day); Tr. Day 3 at 130:21-131:6; Ex. 19A at BPVA-5065-5068 (a January 2013 mental health note stated he was smoking two packs per day and had smoked since 1985). Mr. Bulow continued

[17] At his colonoscopy on November 6, 2015, Mr. Bulow weighed 215 pounds. Tr. Day 1 at 57:9-20; Ex. 19A at BPVA-04706; Ex. 19A at BPVA-04688-04689. In the hospital on November 17, 2015, he weighed 225 pounds. Tr. Day 1 at 92:17-20; 93:9-23.

smoking through November 2015. Tr. Day 2 at 4:22-23; Tr. Day 1 at 39:2-9.

25. Mr. Bulow's long-term alcohol abuse is well documented. His records conflict about precisely when he stopped drinking, but generally support that he stopped drinking more than a year before he developed pancreatitis.[18]

II. CAUSES OF ACUTE PANCREATITIS

A. Common Causes

26. Pancreatitis is inflammation of the pancreas, which can be either acute or chronic but is clinically presented in more of a continuum. Tr. Day 4 at 108:18-109:21. The most common causes of acute pancreatitis are excessive alcohol

[18] Mr. Bulow's psychiatrist in Portland noted in December 2002 that he reported drinking heavily to cope with his troubles and drank two to three ounces of hard alcohol in a mixed drink per night seven days per week. Tr. Day 3 at 128:9-25; Ex. 9A at PVA-0443-446. A September 2007 primary care note mentions alcohol abuse. The narrative reads "Mr. Bulow comes in today with concern for his emotional/physical health. He has been drinking more than usual lately, which was approximately six shots a night, five times a week. He tries to take Sunday, Monday night off from drinking. And when he does, he starts to become very agitated and shaky…. His drinking has progressively gotten worse over the past five to seven years." Tr. Day 3 at 129:1-130:9, Ex. 9A at PVA-0356-0360. In September 2011, Mr. Bulow's primary care physician noted he was drinking about 20 alcoholic drinks per week. Tr. Day 3 at 130:10-20; Ex. 19A at BPVA-05092-05097. Dr. Monroy noted in January 2013 that Mr. Bulow's alcohol use was occasional at the time. Tr. Day 3 at 130:21-131:6; Ex. 19A at BPVA-05065-5068. However, not quite two weeks later, Mr. Bulow visited a private facility called SalusCare or Lee Mental Health Center. A February 8, 2013 intake assessment reads that Mr. Bulow identifies his problem as overusing alcohol and in quotes reads "It's the only way I can relax." It states that he increased alcohol use in 2003, and in February 2013 was consuming four to eight shots of whiskey or rum nightly. Ex. 10A at SC-0012-0016. Mr. Bulow testified that he stopped drinking for a few months in 2011 then restarted, but that he stopped drinking for good in 2013. He testified that he was always honest with his medical providers about how much he was drinking. Tr. Day 3 at 127:17-128:5; 131:12-133:13.

use, gallstones, followed by high triglycerides as the third common cause.[19] Tr. Day 4 at 110:18-113:7 (Tenner); Tr. Day 1 at 207:9-14; 211:13-23; 212:7-10 (Freedman). According to Dr. Scott Tenner, a gastroenterologist and Defendant's expert, these causes are all reversible and make up about two-thirds of the cases. Tr. Day 4 at 110:18-113:7. At least 20 to 40 percent of the cases are idiopathic, meaning that the aforementioned causes are not present and therefore the cause is unknown. Tr. Day 4 at 110:24-25; 113:5-7; 150:19-25.

27. All of the treating physicians and experts agree that Mr. Bulow's acute pancreatitis was not caused by gallstones. Some considered that Mr. Bulow's prior alcohol abuse (pre-2014) may have played a role, but all ruled out alcohol as the cause of the acute pancreatitis.[20] The treating physicians diagnosed the cause as high triglycerides.

28. Mr. Bulow's initial level at the hospital was 972. Plaintiffs' experts testified that only triglyceride levels over 1,000 support a conclusion that the acute

[19] Other causes include a tumor or manipulation from a procedure such as endoscopic retrograde cholangiopancreatography ("ERCP"). Nothing suggests Mr. Bulow had either of these two causes. Tr. Day 4 at 110:18-113:7.

[20] Dr. Freedman testified that long-term chronic alcohol abuse is correlated with an increased risk of acute pancreatitis. Based on *UpToDate*, Dr. Freedman testified that the threshold is generally 50 grams per day. Tr. Day 1 at 202:20-203:1; 214:24-215:22. As Dr. Tenner explained, alcohol by itself cannot cause acute pancreatitis the way gallstones do, but alcohol damages the organ after drinking heavily for five to seven years. He stated the patient may look just like one with gallstone pancreatitis, but the truth is that you really have a patient with alcoholism who chronically scarred their pancreas to the point that they blocked the duct in some way and caused the clinical presentation of acute pancreatitis. Tr. Day 4 at 108:18-109:21.

pancreatitis was caused by hypertriglyceridemia. Tr. Day 1 at 135-37 (Freedman); Tr. Day 2 at 71-76 (Smetana). Both of these experts ruled out elevated, as opposed to high, levels of triglycerides as the cause, particularly since Mr. Bulow had a history of elevated triglycerides. *Id*.

29. With respect to the 1,000 triglycerides threshold, Dr. Freedman acknowledged that he previously presented to the FDA that the risk of pancreatitis and its severity increases along a continuum of elevating triglyceride levels. Tr. Day 1 at 222:4-11; 228:7-12.[21] His presentation to the FDA showed that the risk of pancreatitis increases proportionally with triglyceride levels starting at around 300 mg/dL (milligrams per deciliter). Tr. Day 1 at 224:1-225:17. Dr. Freedman, in the *New England Journal of Medicine*, wrote that "[o]bservational data suggests that the incidence of acute pancreatitis increases approximately 3 percent for every increment of 100 milligrams per deciliter in triglyceride levels over 1,000 milligrams per deciliter." Tr. Day 1 at 221:14-222:3. The Nawaz study, cited by Dr. Freedman, highlighted the differences in the likelihood of increased morbidity and mortality, increased stays in intensive care required by hospital admissions with over 1,000 triglyceride levels, and

[21] Dr. Freedman testified and presented PowerPoint slides to the FDA Endocrinologic and Metabolic Drugs Advisory Committee in Silver Spring, Maryland on May 10, 2018. That committee was considering Volanesorsen, a drug for familial chylomicronemia, which causes hypertriglyceridemia. Neither Volanesorsen nor familial chylomicronemia are at issue in this case, but much of Dr. Freedman's FDA testimony addressed hypertriglyceridemia and acute pancreatitis generally. *See* Tr. Day 1 at 218:7-221:9.

other complications. The Nawaz study, however, looked at patients who had both pancreatitis and high triglycerides, not patients who had triglyceride-induced acute pancreatitis. Tr. Day 1 at 228:7-230:1.[22]

30. Dr. Freedman testified that lipemic serum is the "trigger" for physicians to think about triglycerides as the cause of acute pancreatitis. Tr. Day 1 at 213:9-20. Dr. Freedman testified that for triglyceride-induced pancreatitis, "When you draw someone's blood, they have something called lipemic serum [which] looks like a milkshake [and] usually the triglycerides are astronomical." Tr. Day 1 at 237:13-19, 23-238:12.[23] Per Dr. Freedman, diabetics can have elevated triglycerides that are in the 300-500s. Tr. Day 1 at 212:18-213:8; 227:7-23. Although Plaintiffs' experts could not rule out triglycerides as the cause of the acute pancreatitis, they opined that the cause was more likely than not Depakote. Tr. Day 1 at 234:11-18; 235:21-236:10 (Freedman); Tr. Day 2 at 76:5-11 (Smetana).

B. Uncommon Causes

31. A rare cause of pancreatitis can be illicit or pharmaceutical drugs. Dr. Freedman and Dr. Smetana, Plaintiffs' experts, testified that Depakote can cause

[22] As Dr. Tenner explained, triglyceride levels sometimes go up when a patient has acute pancreatitis. Tr. Day 4 at 116:22-24. Dr. Freedman testified that acute pancreatitis itself can drive up triglyceride levels into the 300s to 500s, maybe as high as 700 or 800. Tr. Day 1 at 227:7-23.

[23] Mr. Bulow's blood work showed lipidic serum at his subsequent December 2015 hospitalization.

pancreatitis. Tr. Day 2 at 77:5-11 (Smetana); Tr. Day 1 at 130:4-131:14 (Freedman). Mr. Bulow's treating physicians—Drs. Fawcett, Barrie, Fernandes, and Lopez-Chaves—testified they knew valproic acid, or Depakote, can be associated with pancreatitis. Tr. Day 2 at 7:14-11:12 (Fawcett); Tr. Day 2 at 24:17-20, 25:13-26-1 (Lopez-Chaves); Tr. Day 1 at 46:3-47:5 (Fernandes); Tr. Day 1 at 71:17-22 (Barrie). Dr. Buffington, Defendant's expert pharmacologist and toxologist, acknowledged that Depakote could be a cause of pancreatitis but ruled it out as a cause in Mr. Bulow's case. Tr. Day 4 at 85:17-86:7; 98:20-99:10 (Buffington). Dr. Tenner testified that there is no study or evidence that shows Depakote, or valproic acid, causes pancreatitis. Tr. Day 4 at 118:15-16; 149-169. Dr. Tenner's opinion is different from the others. Weighing the evidence, the Court recognizes that Depakote may be associated with (as that term is used by medical professionals) pancreatitis but does not find that Depakote was the legal cause here.

32. High triglycerides are often associated with fatty meals and may fluctuate based on the patient's nutritional state. Tr. Day 1 at 62:13-21 (Fernandes); Tr. Day 4 at 116:6-15 (Tenner); Tr. Day 1 at 200:18-201:3 (Freedman); Tr. Day 1 at 100:5-15 (Barrie). The treatment for acute pancreatitis caused by hypertriglyceridemia includes prescribing a patient be "NPO" (be given nothing by mouth) which usually brings down triglycerides. Tr. Day 1 at 232:16-22

(Freedman). Not eating lowers triglyceride levels fairly rapidly. Tr. Day 1 at 61:15-20; Tr. Day 1 at 54:5-55:5; 55:21-56:1 (Fernandes); Ex. 19A at BPVA-04734-04736; Tr. Day 4 at 116:25-117:3 (Tenner).

III. FIRST EPISODE OF ACUTE PANCREATITIS

33. Mrs. Bulow testified that on November 16, 2015, her husband started moaning and complaining, which they first thought was related to his gastrointestinal problems. His condition worsened and they went to the hospital. Tr. Day 4 at 20:20-21:4. Mr. Bulow reported that he had not eaten for at least two days before his hospital admission. Tr. Day 1 at 99:19-25; Ex. 19A at BPVA-04647. When he presented to Bay Pines VA, he was diagnosed with acute pancreatitis.

34. After the emergency room doctor, Dr. George Fawcett, admitted him to the hospital, three physicians treated Mr. Bulow during his three-day stay—Drs. Edwin Lopez-Chaves, Angelo Fernandes, and Sanya Barrie. A nurse practitioner and a clinical pharmacist also treated him while he was in the hospital.

A. Emergency Room Physician Dr. Fawcett

35. Emergency medicine physician Dr. George Fawcett testified that Mr. Bulow presented with severe abdominal pain. Dr. Fawcett took a history, did a physical exam, and ordered lab work and studies, including a CT scan. Tr. Day 2 at 4:13-

18; 6:1-5. He ordered a standard abdominal pain workup, including a complete blood count, complete metabolic panel to check for liver, kidney, and electrolyte disturbances, a coagulation profile to check for potential bleeding, a troponin (heart enzyme), an EKG, and amylase and lipase to check for pancreatic function or pancreatic injury. Tr. Day 2 at 14:14-15:10. Mr. Bulow's lipase was in the 140s, relatively mild elevation, which made acute pancreatitis not yet a "slam-dunk diagnosis." Tr. Day 2 at 6:19-20; 7:14-8:13.

36. Dr. Fawcett testified that a slight elevation in lipase can have several causes, including having passed a gallstone, a pancreatic mass, or inflammation around but not inside the pancreas. The CT scan showed inflammation inside Mr. Bulow's pancreas, confirming acute pancreatitis. Dr. Fawcett diagnosed him with acute pancreatitis with possible pseudocyst development. Tr. Day 2 at 8:14-9:7.

37. Dr. Fawcett was aware that several medications Mr. Bulow was taking were associated with pancreatitis. Tr. Day 2 at 9:8-13. Dr. Fawcett ordered a valproic acid test to see if Mr. Bulow was at a potentially toxic or supratherapeutic level, but it showed Mr. Bulow was at a therapeutic level of Depakote. Tr. Day 2 at 6:12-18; 7:14-8:13. He did not reach a conclusion as to the cause of the pancreatitis. Tr. Day 2 at 16:7-17:6. Dr. Fawcett confirmed the typical care for acute pancreatitis is to admit, rest the bowels, hydrate, and give pain and nausea

medication. Tr. Day 2 at 15:19-16:3. Dr. Fawcett handed off his care to hospitalist Dr. Edwin Lopez-Chaves. Tr. Day 2 at 11:25-13:5.

B. Hospitalist Dr. Lopez-Chaves

38. On the night of November 16, Dr. Lopez-Chaves' initial assessment after conducting a physical examination and reviewing Mr. Bulow's available lab results was consistent with acute pancreatitis. Tr. Day 2 at 21:8-22:12. Dr. Lopez-Chaves went through possible causes of acute pancreatitis. Mr. Bulow reported he had not been drinking alcohol recently, "so possibly that was excluded." Tr. Day 2 at 22:21-24:11. The CT scan was negative for gallstones. Tr. Day 2 at 23:5-24:3. Dr. Lopez-Chaves did not have the benefit of Mr. Bulow's lipid panel lab results which would show his triglyceride levels of 972. Tr. Day 2 at 25:4-6. He explained that mediations are considered as a reason for pancreatitis if you do not find any other reason for pancreatitis. Tr. Day 2 at 28:25-29:5.

39. Dr. Lopez-Chaves' treatment plan was nothing by mouth to rest the bowel, IV fluids, medications, and completing the workup started by the emergency room. Tr. Day 2 at 28:3-8. Dr. Lopez-Chaves was aware in 2015 that valproic acid had been associated with acute pancreatitis, although such association was very uncommon. Tr. Day 2 at 25:13-20. He considered whether to discontinue Mr. Bulow's valproic acid, but his workup had just been started, and stopping

Depakote might cause psychiatric issues for Mr. Bulow based on his bipolar manic, bipolar depression, mood disorder, and PTSD. Tr. Day 2 at 25:13-26:15; 28:9-24. He did not order a psychiatric consult because it was too early in the hospitalization and there was no basis to order one yet. Tr. Day 2 at 26:19-22; 29:6-18. He kept Mr. Bulow on Depakote as well as his other mood-stabilizing medications gabapentin and risperidone. Dr. Lopez-Chaves, the night hospitalist, handed off Mr. Bulow's care to Dr. Barrie, the day hospitalist. Tr. Day 2 at 24:24-25:3.

C. Hospitalist Dr. Barrie

40. Dr. Sanja Barrie is an internal medicine doctor and has been a hospitalist at Bay Pines VA for almost 20 years. Tr. Day 1 at 67:13-18; 83:13-16. Dr. Barrie saw Mr. Bulow on November 17, 2015 and took her own history and physical. Tr. Day 1 at 68:14-69:12.

41. Mr. Bulow's VA record included a computerized problem list with more than 30 entries. Tr. Day 1 at 86:25-89:4; Ex. 19A at BPVA-04644-04645. Mr. Bulow's had mixed hyperlipidemia, meaning elevated triglycerides and elevated cholesterol. Tr. Day 1 at 87:16-88:3. Dr. Barrie testified that Mr. Bulow was on a high-potency statin for cholesterol. Tr. Day 1 at 88:25-89:4. However, as Mr. Bulow admitted during his endocrinology consult, he did not always take his statin. Tr. Day 1 at 98:17-99:5.

42. Mr. Bulow's problem list also included steatosis of the liver, or fatty liver, that can be caused by obesity and alcohol. Dr. Barrie's impression was that both obesity and alcohol may have played a role in the acute pancreatitis. Even though Mr. Bulow's records reported that he stopped drinking, Dr. Barrie testified that he still may have had consequences from his severe drinking history. Tr. Day 1 at 88:4-22. Dr. Barrie noted Mr. Bulow's lipase was elevated, but not terribly high. Tr. Day 1 at 85:17-22; 96:15-25.

43. Apart from the computerized problem list, Dr. Barrie considered COPD, mood disorder, bipolar disorder, PTSD, ADHD, obstructive sleep apnea, back pain, hypertension, and Barrett's esophagus, which can be associated with heavy alcohol use and can lead to cancer. Dr. Barrie noted these diagnoses because she had to think about each and see if she could make them better. Tr. Day 1 at 89:16-90:15; 90:20-25.

44. Dr. Barrie agreed that Mr. Bulow had acute pancreatitis based on his clinical picture, radiating abdominal pain, elevated lipase, and CT scan. She estimated a hospital stay of two to three days. Tr. Day 1 at 69:16-18; 85:17-22; 95:1-96:3. Dr. Barrie continued Mr. Bulow with nothing by mouth except medications. He was taking Depakote for his mood disorder and bipolar disorder with mania in partial remission. Dr. Barrie was generally aware in 2015 that Depakote had a black box warning. Tr. Day 1 at 75:21-23. She was aware then of an

association between valproic acid and acute pancreatitis. Tr. Day 1 at 75:24-76:8.

45. Dr. Barrie considered risks and benefits of stopping Depakote but continued it because Mr. Bulow's records indicated that he had a history of bipolar disorder, including mania, even suicidal thoughts. Had she stopped the medication, she would have been concerned about him going into mania, binge drinking, or committing suicide. Tr. Day 1 at 74:19-75:16. Dr. Barrie decided that keeping Mr. Bulow psychologically stable was in his best interest. Tr. Day 1 at 71:1-16; 72:2-19.

46. Dr. Barrie believed that the cause of Mr. Bulow's pancreatitis was his triglycerides, which were 972. Any weight gain, increase in sugars, and worsening of diabetes can make triglycerides worse. Tr. Day 1 at 86:16-24; 91:17-92:16. Mr. Bulow had all three shortly before his November 2015 acute pancreatitis. *See* Tr. Day 1 at 57:9-20; 92:17-20; 93:9-23; Tr. Day 2 at 122:9-124:7.

47. Dr. Barrie considered that Mr. Bulow had hypertriglyceridemia with a history of alcohol use, high blood sugars, and obesity. After starting Fenofibrate for triglycerides and a diet, Mr. Bulow's pancreatitis improved. After one day of treatment, Mr. Bulow's triglycerides dropped from the 970s to the 700s, while he was still on Depakote. Triglycerides in the 700s are still far over the normal

upper limit, which is in the 100s. In addition, Mr. Bulow's lipase went down from 140 to 30 and amylase was 43; he no longer had acute pancreatitis based on those values.[24] Therefore, Mr. Bulow's acute pancreatitis got better while he was on Depakote. Tr. Day 1 at 72:20-73:14; 105:15-106:4. Because Mr. Bulow got better while still taking Depakote, Dr. Barrie did not think that Depakote had anything to do with his pancreatitis. Tr. Day 1 at 73:19-75:16; 113:10-17.

48. In addition, before Dr. Barrie would discharge a patient with acute pancreatitis, he or she must be able to tolerate food. Usually, patients who still have acute pancreatitis cannot tolerate food and have pain, nausea, or vomiting. Tr. Day 1 at 96:4-14. On November 18, 2015, Mr. Bulow's abdominal pain had improved. He had no nausea or vomiting and was tolerating food.

49. For Mr. Bulow, Dr. Barrie testified that the most important medication was Fenofibrate to lower triglycerides. Tr. Day 1 at 80:24-81:16. Dr. Barrie ordered follow-up visits with Mr. Bulow's primary care doctor and an endocrinologist to be scheduled shortly after his discharge. She was concerned about his triglycerides and weight. Tr. Day 1 at 112:17-113:1. Dr. Barrie explained that it is always possible for a patient to get high sugars, high triglycerides, and have another bout of acute pancreatitis. Tr. Day 1 at 108:2-9. Dr. Barrie instructed

[24] The reference range for lipase is 22 to 51, while the reference ranges for amylase were 29 to 91 or 36 to 128. Tr. Day 1 at 106:2-21; Ex. 19A at BPVA-04626.

Mr. Bulow that he needed to be on a low-fat diabetic diet and not drink alcohol. Tr. Day 1 at 104:15-105:14; Ex. 19A at BPVA-04627. His triglycerides were 774 when he was discharged. Tr. Day 1 at 100:25-102:5; 103:9-15.

IV. SECOND EPISODE OF ACUTE PANCREATITIS

50. Mr. Bulow was admitted to the Bay Pines VA a second time on December 7, 2015. Tr. Day 2 at 83:1-84:18. All nonessential mediation, including Depakote, was stopped. Tr. Day 2 at 84:19-85:1; 19A at BPVA 4392-4397.

51. At this time, Mr. Bulow's triglyceride level exceeded 1300. Mr. Bulow presented with acute pancreatitis, low blood pressure, and acute kidney malfunctioning. Tr. Day 2 at 83:21-84:18. He was intubated, placed on dialysis, and remained in the ICU. His condition worsened over the next months in the hospital, and he developed several debilitating and continuing medical conditions, including a necrotized pancreas. This second hospitalization lasted several months.

V. EXPERT TESTIMONY

52. Both Dr. Freedman and Dr. Smetana conceded that Mr. Bulow had numerous risk factors for pancreatitis on his first admission on November 16, 2015. Tr. Day 1 at 199:19-21; Tr. Day 2 at 111:2-8. The "new onset of diabetes" was one of several key points to consider when assessing the cause of acute pancreatitis. Tr. Day 1 at 138:19-141:1 (Freedman). Smoking is a risk

factor for pancreatitis, particularly with a history of 35 pack years which doubles a patient's risk of acute recurrent pancreatitis. Tr. Day 2 at 111:2-6 (Smetana); Tr. Day 1 at 201:8-202:18 (Freedman). Long-term alcohol abuse appears to be associated with pancreatitis in adults. Tr. Day 1 at 203:7-23; 205:20-207:8 (Freedman). A "long history, usually 10 to 20 years of alcohol abuse" may be a cause of acute pancreatitis. Tr. Day 2 at 126:1-19 (Smetana).

53. Dr. Freedman agreed that the risk factors of alcohol and smoking combined have a greater effect than the sum of either one individually as to patients' risk of developing acute recurrent pancreatitis. Tr. Day 1 at 204:8-12. Dr. Freedman also agreed that triglyceride levels between 500 and 1000mg/dL may predispose patients to pancreatitis. Tr. Day 1 at 204:20-23. He testified that obesity is a risk factor for acute pancreatitis developing into severe pancreatitis. Tr. Day 1 at 204:24-205:19.[25]

54. The Court finds Mr. Bulow had many pre-existing conditions and risk factors, making it extremely difficult to determine one specific cause of his acute pancreatitis in November 2015. He had a history of alcohol abuse, smoking, and obesity. His borderline diabetes worsened to overt diabetes in October 2015,

[25] Dr. Smetana, on the other hand, was unaware whether obesity is a risk factor for developing pancreatitis or whether it affects the outcome of patients who had pancreatitis from other causes. Tr. Day 2 at 111:9-19.

and he gained ten pounds in the first weeks of November 2015. Mr. Bulow started Depakote in 2013 and continued, on and off, through 2015. His triglycerides fluctuated and spiked once—to over 1100—throughout this period. Dr. Freedman's testimony that hypertriglyceridemia as a cause of acute pancreatitis cannot be considered unless the threshold level of 1,000 is reached was successfully challenged when he opined about acute pancreatitis resulting from hypertriglyceridemia in the neighborhood of 500 to 1,000 dL.

55. The treating physicians, and Plaintiffs' two experts, ruled out gallstones and alcohol, leaving the next most likely cause as hypertriglyceridemia. Plaintiffs' experts could not rule out hypertriglyceridemia. His triglycerides responded appropriately to the NPO regimen in the hospital—the entire time taking Depakote at the therapeutic level. Even assuming Mr. Bulow took the Depakote as prescribed in August 2015, which is not borne out by the testimony, the expert testimony about the latency theory—that acute pancreatitis presents three to six months after taking Depakote—was successfully challenged. The Court finds credible Dr. Smetana's and Dr. Tenner's testimony that the latency studies show the timeframe can range from several days to years. The black box warning reports cases shortly after initial use to several years. The three months from August to November 2015 does not indicate either way that Depakote was the cause.

56. The Court further finds neither Dr. Freedman's nor Dr. Smetana's testimony credible with respect to various studies and reports on Depakote. First, the black box warning does not state that Depakote can cause pancreatitis; it discusses case reports. The Court finds the treating physicians' and Defendant's expert testimony credible that Depakote can be associated with, as opposed to the cause of, pancreatitis. Dr. Freedman's testimony is particularly unconvincing about studies showing Depakote as the cause of pancreatitis. The Court finds credible the testimony of Defendant's expert, Dr. Tenner, that there is no data or epidemiological evidence showing that Depakote causes acute pancreatitis.

CONCLUSIONS OF LAW

Based upon the findings of fact, the Court reaches the following conclusions of law:

57. Florida law applies in this medical malpractice claim brought against the United States for the alleged medical treatment by VA physicians under the Federal Tort Claims Act, 28 U.S.C. § 2671 *et. seq*. *Stone v. United States*, 373 F.3d 1129, 1130 (11th Cir. 2004).

58. To prevail in a medical malpractice case, the plaintiff must establish the standard of care owed by the defendant, the defendant's breach of that standard, and the proximate cause as the breach resulting in damages. *Saunders v. Dickens*, 151 So. 3d 434, 441 (Fla. 2014); *Gooding v. Univ. Hosp. Bldg.*, 445 So.

2d 1015, 1018 (Fla. 1984). The plaintiff "must prove each element by a preponderance of the evidence, meaning 'more likely than not.'" *Saunders*, 151 So. 3d at 442.

VI. STANDARD OF CARE

59. A physician's duty requires that he or she act within the standard of professional care. § 766.102, Fla. Stat. "The standard of professional care is a level of care, skill, and treatment that, in consideration of all surrounding circumstances, is recognized as acceptable and appropriate by similar and reasonably prudent health care providers." *Saunders*, 151 So. 3d at 441. The plaintiff must establish that the care provided fell below that of a reasonably prudent physician. *Id.* at 442.

60. In this case both clinical guidelines and expert testimony were presented to establish the standard of care.

A. Clinical Guidelines and Expert Testimony

61. Five sets of clinical guidelines have been published concerning the treatment of acute pancreatitis. Tr. Day 1 at 160:18-162:16 (American Gastroenterological Association, American College of Gastroenterology, International Association of Pancreatology, American Pancreatic Association, and American Society of Gastrointestinal Endoscopy). None of them require stopping Depakote upon admission with acute pancreatitis.

62. Plaintiffs' expert Dr. Freedman reviewed these five sets of guidelines in an article he co-authored in 2019. Tr. Day 1 at 156:25-158:24. The article made no mention of stopping any medication as a quality of care indicator. Tr. Day 4 at 147:4-5. The guidelines did not recommend that medications associated with pancreatitis based on case reports be stopped upon developing acute pancreatitis. Tr. Day 4 at 107:6-19. Nevertheless, Dr. Freedman opined that the standard of care "would have been to note that Depakote potentially is the cause of the pancreatitis here and to stop it . . . or to justify why it shouldn't be stopped." Tr. Day 1 at 144.

63. Defendant's expert Dr. Tenner was lead author of the guidelines published by the American College of Gastroenterology, which do not direct the stoppage of all medications with an association to acute pancreatitis, nor do they state to stop Depakote in particular. Tr. Day 4 at 106:15-107:2; 144:2-4; 144:16-24; Tr. Day 1 at 49:3-14. Moreover, Dr. Tenner opined that the VA doctors satisfied the four quality of care indicators listed in Dr. Freedman's article: ordered liver function test within 24 hours, conducted ultrasound within 48 hours, documented alcohol use, and measured triglycerides. Tr. Day 4 at 146:12-25. The Court finds Dr. Tenner's testimony more credible in setting the standard of care. As stated by Dr. Tenner, the standard of care does not require a patient to be removed from Depakote upon developing acute pancreatitis, and particularly

not on the first admission of the patient with acute pancreatitis. Tr. Day 4 at 142-45.

64. Dr. Freedman conceded that hypertriglyceridemia must be treated first before stopping medications that might potentially be the cause. Tr. Day 1 at 242:19-245:8. The VA physicians treated Mr. Bulow's hypertriglyceridemia and his pancreatitis improved. Applying the standard of care, the VA physicians ruled out gallstones, alcohol abuse, and tumors, leaving triglycerides as the most likely cause. Mr. Bulow's positive response to the treatment negated further need to stop any of his 15 total medications. Even Drs. Freedman and Smetana could not rule out hypertriglyceridemia as the cause.

B. FDA Black Box Warning

65. All of the witnesses who were asked agreed that a black box warning does not set the standard of care. Tr. Day 1 at 154:22-155:9 (Freedman); 64:12-19 (Fernandes); 75:21-77:15 (Barrie); Tr. Day 2 at 80:3-17 (Smetana); Tr. Day 4 at 142:25-143:4 (Tenner); Tr. Day 4 at 61:8-9; 63:5-9; 70:14-71:5; 76:20-77:3 (Buffington).

66. In any event, the Court finds that the VA physicians did not ignore the black box warning when they did not take Mr. Bulow off Depakote. They all testified they were aware in 2015 that Depakote can be associated with pancreatitis, but Mr. Bulow responded to the high triglyceride treatment. Dr. Barrie added that

there was a risk of mental instability if Depakote was stopped.[26]

67. The 972 level, although below 1,000, could be the cause based on Dr. Freedman's own testimony regarding the correlation between increasing triglycerides and the increasing risk of pancreatitis—a continuum. Plaintiffs did not prove that the threshold of 1,000 was the definitive factor of diagnosing triglycerides as the cause of pancreatitis. As Dr. Tenner opined, Mr. Bulow had a significant history of alcoholism and a triglyceride level "around a thousand." Tr. Day 4 at 147-48. There is "no magic line" for the triglyceride threshold, and levels over 700 and 800 should be entertained. *Id*. at 148. Because any damage to the pancreas caused by his prior alcohol use and continued tobacco use could not be treated, the triglycerides should be treated on the first admission. *Id*. at 147-48. Weighing the credibility of witnesses and the evidence, the Court finds the treating physicians did not breach the standard of care by not taking Mr. Bulow off Depakote at or during his first admission in November 2015 or at that November discharge two to three days later.

VII. BREACH OF STANDARD OF CARE

68. As discussed above, the VA physicians ruled out and treated the common causes before stopping a medication, which was not commonly correlative with

[26] The fact section above sets forth Mr. Bulow's long struggle with mental issues, particularly the prevalence of suicidal thoughts and angry outbursts.

rare, uncommon causes of pancreatitis. In 2015, there had been only 120 case reports of Depakote-associated acute pancreatitis out of millions of Depakote prescriptions. Tr. Day 1 at 63:25-64:6 (Fernandes). Because Mr. Bulow responded to the treatment for lowering triglycerides, and his risk factors all led to the conclusion that elevated triglycerides were more likely than not the cause of the acute pancreatitis, Plaintiffs have failed to prove the standard of care was breached.[27] Mr. Bulow's triglycerides had been in the 400s and 500s for some time, he had put on sudden, substantial weight, his diabetes became overt in October, and he had not been routinely taking his statin. The fact that he began taking Depakote again in August 2015, after having taken it on and off since 2013, did not establish Depakote as the contributing medical cause. The latency data did not establish that any particular time frame (and not a specific threeto six-month period as posited by Plaintiffs) applied to Depakote-associated pancreatitis.

VIII. CAUSATION

69. To determine whether any breach of the prevailing professional standard of care proximately caused the injury, the plaintiff must show "that what was done or failed to be done probably would have affected the outcome." *United States*

[27] Plaintiffs have not proven that his pancreatitis was the cause of his raised triglycerides because both Dr. Freedman and Dr. Fernandes testified that while acute pancreatitis can increase triglycerides, it does not raise them as high as 972.

Chiarino, 189 F. Supp. 3d 1371, 1384 (S.D. Fla. 2016) (citing *Santa Lucia v. LeVine*, 198 So. 3d 803, 809 (Fla. 2d DCA 2016) (quotation citation omitted). Florida follows the "more likely than not" standard for causation. *Saunders*, 151 So. 3d at 441. Courts must decide "whether said injury, given actual causation, was a foreseeable consequence of the danger created by the defendant's negligent act or omission." *Ruiz v. Tenet Hialeah Healthsystem, Inc*., 260 So. 3d 977, 981–82 (Fla. 2018) (citation omitted). "A harm is 'proximate' in a legal sense if prudent human foresight would lead one to expect that similar harm is likely to be substantially caused by the specific act or omission in question." *Ruiz*, 260 So. 3d at 982 (citation and internal quotation marks omitted).

70. A plaintiff must show both general and specific causation: A) the drug can potentially cause a particular disease (general); and B) the drug actually caused the plaintiff's disease (specific or individual). *Chapman v. Procter & Gamble Distributing, LLC*, 766 F.3d 1296, 1306–1311 (11th Cir. 2014); *Guinn v. AstraZeneca Pharms. LP*, 602 F.3d 1245, 1248 n.1 (11th Cir. 2010); *McClain v. Metabolife Intern., Inc*., 401 F.3d 1233, 1237 (11th Cir. 2005).

A. General

71. Three primary methods are used to prove general causation, along with several other secondary methods. *Chapman*, 766 F.3d at 1307–08; *In re Abilify (Aripiprazole) Prods. Liab. Lit.*, 299 F. Supp. 3d 1291, 1306 (N.D. Fla. 2018).

The primary methods include knowledge of dose-response, epidemiological evidence, and background risk of disease. *Id*. The secondary methods include plausible explanations, generalized case reports, hypotheses, and animal studies. *Id.*

72. A general causation opinion that is not supported by at least one primary methodology is unreliable as a matter of law. *Chapman*, 766 F.3d at 1308. With respect to the methodology of dose-response, there is no known daily or quantitative dose of Depakote above which a patient is at risk for pancreatitis. Tr. Day 1 at 198:16-199:18 (Freedman); Tr. Day 4 at 142:14-24; 132:18-21 (Tenner).

73. "Epidemiology is the best evidence of causation in cases involving toxic substances." *Chapman*, 766 F.3d at 1307 (internal quotation marks omitted). Randomized clinical trials and observational studies fall into the category of epidemiological evidence. Reference Manual on Scientific Evidence (3d. ed. 2011) ("Ref. Man.") at 551, 558-560. Even if Plaintiffs had put forth evidence showing that Depakote was associated with acute pancreatitis in an epidemiological study, which Plaintiffs did not, the analysis would not end there. The next step would be to consider whether that association was causal based on the Bradford Hill criteria. Ref. Man. at 597-600; *see also In re Abilify*, 299 F.

Supp. 3d at 1307 (considering Bradford Hill factors).[28]

74. An association "describes the relationship between two events that occur more frequently together than one would expect by chance. Association does not necessarily imply a causal effect. Causation is used to describe the association between the two events when one event is a necessary link in a chain of events that results in the effect." Ref. Man. at 552-553, n.7. Dr. Tenner explained the difference between proximate cause in the law and causation in medicine. Tr. Day 4 at 140-41. A correlation or association between a drug and a condition is not causation. A drug's association with a medical condition does not mean the drug caused the condition.

75. Dr. Tenner considered the application of the Bradford Hill criteria to Depakote and acute pancreatitis. Tr. Day 4 at 139-149. He explained that there is "no biologic plausibility of how Depakote would cause pancreatitis," as opposed to the known mechanism of how tobacco causes lung cancer. Tr. Day 4 at 142. He confirmed no medical evidence showed that Depakote causes acute pancreatitis. *Id*. at 152.

76. The Court finds Dr. Tenner's testimony makes more sense than Dr.

[28] "Sir Austin Bradford Hill was a world-renowned epidemiologist who articulated a nine-factor set of guidelines that is widely accepted in the scientific community for determining whether an observed association between an agent and a disease reflects a true causal relationship." *In re Abilify*, 299 F. Supp. 3d at n.19.

Freedman's. Dr. Freedman's attempt to state causation is *ipse dixit*. He, along with Dr. Smetana, relied on secondary methods of proving general causation, which may not stand alone as proof; secondary methods may only be used to support primary methods of proof. *See Chapman*, 766 F.3d at 1307-08; *In re Abilify*, 299 F. Supp. 3d at 1306. Case reports (involving one patient) or case studies (involving a small number of patients) "are merely accounts of medical events" in an uncontrolled context that "do not rule out the possibility that the effect manifested in the reported patient's case is simply idiosyncratic or the result of unknown confounding factors." *McClain*, 401 F.3d at 1253–54 (quoting *Rider v. Sandoz Pharmaceuticals*, 295 F, 3d 1194, 1199 (11th Cir. 2002)).

77. Dr. Freedman relied on 90 case reports, 53 publications, the FDA black box warning, and multiple rechallenge case reports.[29] Tr. Day 1 at 184:25-185:6; 202:2-9. Dr. Smetana relied on the FDA black box warning and articles, which analyzed case reports. Tr. Day 2 at 105:24-106:4. Under the applicable case law, reliance on secondary methods does not constitute proof that Depakote causes acute pancreatitis. The evidence presented here failed to show that Depakote, more likely than not, is a cause of acute pancreatitis. Accordingly,

[29] Rechallenging case reports are based on a patient's stopping a medication and then later restarting it to see if the same condition, such as pancreatitis, recurs. Tr. Day1 at 132–33.

Plaintiffs failed to show general causation by the greater weight of the evidence.

B. Specific

78. In addition to the deficiencies in Plaintiffs' experts' methodology, Mr. Bulow's prior problems impaired Plaintiffs' attempt to show specific causation—that Depakote was the actual cause of Mr. Bulow's pancreatitis in either November or December 2015.

79. Mr. Bulow's numerous risk factors for acute pancreatitis make it difficult to draw any inference regarding specific causation. He was obese and had developed overt diabetes about one month before his November 2015 admission. He was a life-long smoker and a heavy drinker until 2013, such that his pancreas probably suffered irretrievable damage, as all the doctors agreed.

80. Mr. Bulow took Depakote as early as April 2013. He weaned himself off at some point in 2015 and restarted in August 2015, yet his triglycerides fluctuated in the 300s to 500s the entire time, with the exception of a sudden spike to over 1,000 in March 2015. This evidence shows no correlation between taking Depakote and his triglyceride levels from 2013 to November 2015, particularly given the inability of Plaintiffs' experts to prove that a three-to six-month latency period, or a rechallenging event, applied to the relationship between Depakote and pancreatitis or to establish that the FDA black box warning required stoppage of Depakote.

81. Mr. Bulow's condition improved greatly during the first, November 2015 hospital stay. The VA physicians left him on Depakote to stabilize his mood, based on his lengthy history of bipolar disorder, anger outbursts, and recent suicidal thoughts. The VA physicians were aware of a possible association between Depakote and pancreatitis. They were also aware that no reliable studies dictated stoppage of Depakote if triglycerides increased to a level of less than 1,000— the absolute threshold posited by Plaintiffs' experts. On the continuum testified to by all experts, the jump from around 300s to 500s all the way to 972 is more than substantial to merit ruling out high triglycerides as a cause before removing Depakote from Mr. Bulow's 15 medications. The VA physicians did not breach the standard of care, nor was general or specific causation proven.

82. This same conclusion is more compelling for Mr. Bulow's December 2015 hospital admission. Mr. Bulow presented to the hospital with triglycerides of 1362, which, even according to Plaintiffs' experts, represented a classic case of pancreatitis caused by high triglycerides (over 1,000). The lipidic serum was also present in Mr. Bulow's blood, which was another strong indicator of pancreatitis cause by hypertriglyceridemia per Dr. Freedman's testimony. Having determined the Defendant's expert Dr. Tenner more credible than the Plaintiffs' experts and weighing all the evidence, the Court finds for the

Defendant.

Accordingly, the Clerk is directed to enter final judgment in favor of Defendant and thereafter close the case.

DONE AND ORDERED at Tampa, Florida, on December 22, 2021.

WILLIAM F. JUNG
UNITED STATES DISTRICT JUDGE

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Counsel of record